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Visual Function and Subjective Perception of Vision following bilateral implantation of monofocal and multifocal intraocular lenses: A Randomised Controlled Trial

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Abstract:	PURPOSE: Following implantation with Multifocal intraocular lenses (MIOLs) or monofocal intraocular lenses (IOLs), the study examines monocular and binocular visual function and patient reporting outcomes using a rigorous series of clinical assessments. Setting: BMI Southend Hospital, UK DESIGN: Prospective, randomised, double-masked clinical trial. METHODS: 100 subjects were randomised for bilateral implantation of either Bi-Flex 677MY MIOL or Bi-Flex 677AB IOL and were assessed at 3-6 months (V1) and 12-18 months (V2). Primary outcomes included distance, intermediate and near LogMAR visual acuities (VA) and defocus curve profile assessment. Secondary outcomes included reading speed, contrast sensitivity (CS) and the subjective perception of quality-of-vision. RESULTS: Uncorrected (MIOL 0.10±0.09LogMAR; IOL 0.09±0.11LogMAR) and best distance-corrected VA (MIOL 0.04±0.06LogMAR; IOL 0.01±0.07LogMAR) were comparable ($p > 0.05$). Unaided near VA (UNVA $p<0.001$: MIOL 0.23±0.13LogMAR; IOL 0.55±0.20LogMAR) and distance-corrected near VA (DCNVA $p<0.001$: MIOL 0.24±0.13LogMAR; IOL 0.54±0.17LogMAR) were significantly improved with MIOLs. There was no significant difference in distance-corrected intermediate VA (DCIVA $p=0.431$: MIOL 0.38±0.13; IOL 0.39±0.13). Defocus curves demonstrated an increased range-of-focus amongst MIOLs (MIOL 4.14±1.10D; IOL 2.57±0.77D). Pelli-Robson CS was different at V1 ($p < 0.001$) but similar by V2 ($p = 0.059$). Overall satisfaction was high (>90%) in both groups for distance tasks whereas significantly different for near (MIOL 18.45±16.53LogUnits; MIOL 55.59±22.52LogUnits). CONCLUSIONS : Unaided near visual acuity is demonstrably better with MIOLs and there was greater subjective satisfaction with their quality-of-near-vision. Halos reported by the MIOL group was significant compared to the IOL group, but did not show an adverse effect on overall satisfaction.

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Dear Prof Mamalis,

Thank you for reviewing of our manuscript. Please see below our responses to the comments highlighting our revisions that have been made to the manuscript

Reviewers' comments: Reviewer #1: The authors have responded to the various issues raised in my initial review and inserted comments accordingly in the article.
Although this paper does not offer an original comparison (monofocal versus multifocal), it offers the advantage of a beautiful prospective methodology, which can be used as a reference in particular for the defence of multifocal optics before the authorities of the various ministries of health, eager for quality scientific evidence.

Thank you for your review

Editors comments: Would the space constraints be met if we made all of the tables (there are seven of them) online only but kept all of the figures? Yes, the tables could be made online only and the figures could all be kept as long as they are all one column.

Thanks for your answer to our query.

We have changed the figures in order for them to keep to a single column. To do this we have separated the Visit 1 and Visit 2 graphs and are only presenting the visit 2 data in the main manuscript. The Visit 1 graphs are now online only along with all the data within the tables (supplementary material).

Kind regards

Phill

Dr Phillip Buckhurst

Associate Professor | Associate Dean for Research | Associate Head of School (Research)

Visual Function and Subjective Perception of Vision following bilateral implantation of monofocal and multifocal intraocular lenses: A Randomised Controlled Trial.

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Running Head: Visual Function with MIOLs

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ABSTRACT

PURPOSE:

Following implantation with Multifocal intraocular lenses (MIOLs) or monofocal intraocular lenses (IOLs), the study examines monocular and binocular visual function and patient reporting outcomes using a rigorous series of clinical assessments.

Setting: BMI Southend Hospital, UK

DESIGN: Prospective, randomised, double-masked clinical trial.

METHODS: 100 subjects were randomised for bilateral implantation of either Bi-Flex 677MY MIOL or Bi-Flex 677AB IOL and were assessed at 3-6 months (V1) and 12-18 months (V2). Primary outcomes included distance, intermediate and near LogMAR visual acuities (VA) and defocus curve profile assessment. Secondary outcomes included reading speed, contrast sensitivity (CS) and the subjective perception of quality-of-vision.

RESULTS: Uncorrected (MIOL 0.10±0.09LogMAR; IOL 0.09±0.11LogMAR) and best distance-corrected VA (MIOL 0.04±0.06LogMAR; IOL 0.01±0.07LogMAR) were comparable (p>0.05). Unaided near VA (UNVA p<0.001: MIOL 0.23±0.13LogMAR; IOL 0.55±0.20LogMAR) and distance-corrected near VA (DCNVA p<0.001: MIOL 0.24±0.13LogMAR; IOL 0.54±0.17LogMAR) were significantly improved with MIOLs. There was no significant difference in distance-corrected intermediate VA (DCIVA p=0.431: MIOL 0.38±0.13; IOL 0.39±0.13).

Defocus curves demonstrated an increased range-of-focus amongst MIOLs (MIOL 4.14±1.10D; IOL 2.57±0.77D). Pelli-Robson CS was different at V1 (p<0.001) but similar by V2 (p=0.059).

Overall satisfaction was high (>90%) in both groups for distance tasks whereas significantly different for near (MIOL 18.45±16.53LogUnits; MIOL 55.59±22.52LogUnits).

CONCLUSIONS: Unaided near visual acuity is demonstrably better with MIOLs and there was greater subjective satisfaction with their quality-of-near-vision. Halos reported by the MIOL group was significant compared to the IOL group, but did not show an adverse effect on overall satisfaction.

Multifocal intraocular lenses (MIOLs) are widely considered the most reliable method of achieving spectacle independence following cataract surgery.[1-3] MIOLs distribute the light between distant and near focal points whereby the vergence of the incident light dictates which focal point is conjugate to the retinal plane.

The separation of these multiple focal points is determined by the addition power of the MIOL and to a lesser extent the biometry of the eye. High addition MIOLs (+4.00D or higher) are the zeitgeist of the designs used in the late 90s-early 2000s. Disadvantages of these early lenses included a close working distance and reduced intermediate vision. Moreover, the size of the dysphotopic phenomenon (commonly described as halo), associated with MIOLs, increases according to the addition power; these higher addition lenses generate larger haloes.[4,5]

The light energy distribution between the retinal focal points created by a MIOL influences the overall quality of vision at different viewing distances. MIOLs that split light equally, create two focal points of comparative image quality. In contrast, distance dominant MIOLs allocate a higher

percentage of light towards the distance retinal focal point and consequently near vision is relatively compromised. Conversely, the intensity of the halo is influenced by the light distribution relationship: the more distance dominant the lower the dysphotopic intensity.

In 2016, a Cochrane Review[6] highlighted the need for robust randomised control trials examining the efficacy of MIOLs over monofocal intraocular lens (IOL) implantation and called for standardization of outcome measures in MIOL studies. The review concluded that it was unclear whether the achieved benefits of MIOL implantation i.e. greater near vision and increased spectacle independence, outweighed disadvantages such as reduced contrast sensitivity and increased dysphotopsia. Subsequently others have also highlighted the importance of patient reported outcomes in MIOLs.[7] Despite these conclusions, in the subsequent three years there has only been a single RCT published comparing MIOLs with IOLs.[8]

The present study compared the efficacy of the Bi-Flex 677MY MIOL over its parent monofocal IOL using standardized methods for assessing both visual function and the subjective perception of the quality of vision.

METHODS

This study was a prospective, parallel double masked randomised clinical trial. The study protocol adheres to the Declaration of Helsinki and ethical approval was obtained prior to commencement of the trial. The study was registered with clinicaltrails.gov (NCT02338882) and written consent was obtained from all subjects. No modifications to the protocol or outcome measures were

made during the study. The aim was to assess the IOLs using recognised methods that would provide rigour and establish a comprehensive method which could be utilised with all IOLs and allow easy comparison of results.

Patient Selection

Between September 2015 and May 2017, one hundred subjects were recruited from routine cataract clinics at the BMI Southend Hospital on a consecutive – if – eligible basis according to the inclusion/exclusion criteria (Supplementary Table 1). All subjects underwent initial examination by a consultant ophthalmic surgeon including dilated fundus examination; in the event of suspected macular pathology an OCT was carried out and if pathology was detected, the patient was excluded as per the study criterion. The anterior segments and ocular surface were also evaluated to confirm lack of pathology and minor ocular surface dryness was treated by commencement of ocular lubricants. Any ocular surface disease deemed moderate or marked resulted in exclusion. The allocation of IOLs was randomly designated and was masked to both the participant and the investigator conducting the post-operative study assessments. On enrolment, a study number was assigned to each subject. Using this study number, the allocation of lenses for all subjects was randomized in Microsoft Excel using blocked randomization with a 1:1 allocation ratio. Following allocation of the subject number, the unmasked surgeons and theatre staff accessed the randomization log and a series of sealed opaque envelopes that described which lenses were to be implanted (MIOL or IOL).

Surgical Technique

All surgeries were performed by one of two experienced consultant ophthalmic surgeons (RA and HK) using small incision phacoemulsification. The same surgeon implanted both lenses for an individual subject. In each case, a 2.2mm clear corneal incision was located according to the steepest corneal meridian. The pre- and post-operative medication regime was the same regardless of surgeon. Second eye surgery occurred within 4 weeks of first eye surgery.

Masking

All post-operative study outcome measures were collected by a study investigator, who was masked to the allocation of study group. The subjects were also masked to their grouping allocation and were only informed of the type of lens implanted once they had completed the study. Post-operative slit lamp examination was performed by the unmasked consultant surgeon in order to maintain masking of the study investigator.

Intraocular Lenses

Each group had fifty subjects assigned. The Bi-Flex 677 AB is a single piece, aspheric aberration neutral IOL. The Bi-Flex MY MIOL has the same platform as the monofocal but the anterior surface has a 3mm apodized, diffractive central region with a near addition of 3.50D at the IOL plane (Supplementary Table 2). The Bi-Flex MY MIOL design is intended to provide distance dominance with greater mydriasis, thus maximizing contrast and minimizing halos when driving at night. Pupil miosis changes the light distribution relationship and results in a relatively equal split of light, hence, the Bi-Flex MY MIOL exploits the near miosis that occurs with reading. This type of MIOL was chosen for the study given that the unique aspect of the Bi-Flex MY is its low number of diffractive echelons (seven) which is theorized to improve the optical image quality of

the resultant image. The identical platform and material of the two IOLs allowed unhindered assessment of the multifocality.

Primary Outcomes Measures

A masked investigator assessed the subjects at two study visits, 3-6 months (V1) and 12-18 months (V2) post-operatively. At each visit, monocular and binocular LogMAR acuities for unaided distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) were measured using computerised test charts (Thomson Software Solutions Ltd) at 6m following the Bailey-Lovie principles and employing Sloan letters consistent with testing methods established by the Early Treatment Diabetic Retinopathy Study (ETDRS).[9-13] Subjective refraction was conducted at 6m with a distance fixation target. The assessment of unaided near visual acuity (UNVA), distance corrected near visual acuity (DCNVA) and distance corrected intermediate visual acuity (DCIVA) utilised ETDRS charts for near (40cm) and intermediate (70cm) (Precision Vision) working distances respectively. To further assess intermediate and near vision at a range of distances, defocus profiles were plotted from -5.00D to 1.50D in 0.50D steps.[14] The letters and defocus lenses were randomised between measures and subjects were prompted once using the phrase “can you read any more letters on the line below?”.[15] All measures of visual acuity were performed with illuminance 120 cd/m2 and luminance of 95 lux.

Secondary Outcome Measures

Contrast Sensitivity was assessed binocularly with the CSV-1000 (Precision Vision) calibrated to 2.4m and both monocularly and binocularly using Pelli-Robson charts at 6m (Thomson Software). Radner reading charts were used to assess reading speed at 40cm following the method outlined by Radner using a digital stopwatch.[16] The subjective perception of vision was assessed using a quality of vision questionnaire[17] and NAVQ.[18] The Carl Zeiss Meditec Glare simulator was used to quantify the appearance of halos and glare. All secondary measures were assessed at V1 and V2. The same assessment room was used throughout the study and all secondary tests were carried out by the same masked investigator in photopic light conditions of illuminance 120cd/m^2 and luminance of 95 lux.

Statistical Analysis

The sample size for the study was calculated using G*power3 (University of Dusseldorf). Power calculations were based on a medium effect size (f = 0.30) based on *a-priori* matched paired *t test* design and a desired statistical power of 90% with an error probability of 0.05. Statistical analysis was performed using SPSS software, version 24 (IBM). All data were tested for normality using the Shapiro-Wilks test and visual examination of histogram plots. In all instances $p<0.05$ was considered statistically significant. It order to evaluate effect size, Cohen's d was calculated, with $d > 0.2$, 0.5 and 0.8 corresponding to small, medium and large effect sizes, respectively.

A repeated measures ANOVA was used to establish similarity between right and left eye data for both monofocal and multifocal IOL data. No significant differences were found and as such only right eye data is presented.[19] Where differences were found after repeated measures ANOVA, further pairwise tests were used to compare the monofocal and multifocal groups for all visual

acuity and contrast sensitivity measurements. Conversion of the NAVQ results to a Rasch score allowed significance to be determined with a Wilcoxon rank-sum test.

The Radner reading speed data was fitted with a non-linear regression (exponential rise to a maximum). Maximum reading speed (MRS) was defined as the asymptote of this curve and Critical print size (CPS) was calculated as the value for x (print size) when the reading speed was 95% of the MRS.

$$x = \frac{\text{Log}(1 - (y-c/a)}{b} \qquad \text{equation 1}$$

Three methods were used to describe the defocus curves using the metrics published by Buckhurst et al.[20] After accounting for magnification of the defocus lenses, the direct comparison method determined significance at each level of acuity; a two way repeated measures ANOVA and pairwise comparison was used to determine if there was a significant difference between groups. Subsequently, fitting spline curves to the dataset allowed the calculation of the range-of-focus, determined using 0.3LogMAR as the threshold. Finally, the near, intermediate and distance areas of the curve were calculated using 0.3LogMAR as the upper limit.[20]

RESULTS

Patient Demographics

Ninety subjects completed the study, one subject had a surgical complication (posterior capsular rupture) prior to IOL insertion and was thus excluded from the study. All subjects attended the

initial post-operative assessment with the consultant surgeon 3-4 weeks post-surgery, however nine subjects were lost to follow up thereafter, seven of these were excluded due to failure to attend one or both of their study visits despite repeated requests, one failed to attend due to ill health and the remaining subject was deceased (Figure 1). There were no adverse or serious adverse events reported in any subjects.

There were no significant differences in pre-operative measures between subjects in the monofocal IOL and MIOL groups, $p > 0.05$ in all instances (Supplementary Table 3).

Post-Operative Refraction

For all participants, manifest spherical equivalent (MSE) was calculated and astigmatism was analysed using the power vector method as described by Thibos.[21] The effect of uncorrected astigmatism[22] is known to be detrimental to outcomes and as such vector analysis was used to ensure that astigmatic effect was similar between groups. No significant differences were found between groups ($p > 0.05$) (Supplementary Table 4).

Visual Acuity

Significant differences were found for UNVA ($p < 0.01$) and DCNVA ($p< 0.01$) both monocularly and binocularly at V1 and V2. With near visual acuity being significantly better in the MIOL group. No significant difference was found for intermediate vision (70cm) (Figure 2)(Supplementary Figure 1)(Supplementary Table 5).

Defocus

A two-way repeated measure ANOVA was performed and a significant difference found ($F_{1,28}$ = 131.889 $p < 0.001$). Pairwise comparisons identified that the differences were significant through the defocus range -2.00 to -5.00 ($p < 0.001$) at both visits, monocularly and binocularly (Figure 3)(Supplementary Figure 2). Cohen's D effect size was calculated and remained > 1 throughout this range, thus categorized as a large effect size.

Defocus curves were also analysed using the area under the curve method as previously described.[20] MATLAB R2017b (The Mathworks Inc) curve fitting software was used to fit a spline curve to each data set. The same software was then used to calculate the area below the curve assuming y = 0.3LogMAR. The ranges were divided into distance (-0.5 to +0.5 defocus), intermediate (-0.5 to -2.0D defocus) and near (-2.0 to -4.0D defocus). A cut-off value of 0.3LogMAR was used as this is the UK, European and American binocular visual acuity driving standards.[23,24]

Distance area was significantly greater in the monofocal group at Visit 1 but not at Visit 2, no difference was found in the intermediate area but the MIOL group showed a larger near area at both visits. In addition to the area metrics, range of focus was calculated as the dioptric range where VA was ≥ 0.3 LogMAR, by finding the roots of the spline curve fitted. The MIOL group had a significantly larger range of focus ($p<0.001$) (Figure 4)~~,~~(Supplementary Figure 2) (Supplementary Table 6).

Reading Speed

There was significantly better critical print size (CPS) and reading acuity achieved in the MIOL group at V1 (p<0.001) and V2 (p<0.001). No significant difference in MRS was found at either visit (p=0.534 V1 and p =0.555 V2) (Figure 5) (Supplementary Figure 4).

Contrast Sensitivity

Monocular and binocular measures of contrast sensitivity with the Pelli-Robson charts showed a significant difference (p<0.001) at Visit 1 with a large effect size demonstrated (Cohen's d = 0.845 and 1.031 respectively) (Supplementary Figure 5). However, at Visit 2, there was no significant difference between groups when tested binocularly (p = 0.059) (Figure 6).

Binocular contrast sensitivity, measured with the CSV-1000, was greater in the IOL group at visit 1 when measured at 3, 6 and 12cpd spatial frequencies (Supplementary Figure 6); this difference was only present for 12 and 18cpd at Visit 2 (Figure 7)(Supplementary , Table 7).

Prior to visit 1 no subject underwent YAG capsulotomy whereas by visit 2; in the monofocal group one subject required YAG capsulotomy unilaterally and one bilaterally, and in the multifocal group one subject required YAG capsulotomy unilaterally and three required it bilaterally. No post-operative procedures were preformed, for the correction of residual ametropia, on any of the subjects.

Questionnaire

75% of the MIOL group were completely spectacle independent compared to 6.7% of the monofocal group at Visit1. At Visit 2, 66.7% and 4.7% respectively remained completely spectacle independent ~~((~~(Supplementary Figure 7).~~Figure 8a, 8b).~~

The type of spectacles worn in both groups was different post-operatively compared to pre-operatively with fewer subjects using bifocals or varifocals. Single vision near spectacles (reading only) were the most common refractive correction in both groups. A small proportion of subjects used spectacles for distance; this finding was consistent with the satisfaction results. In addition 2.5% of the MIOL group used varifocal spectacles post-operatively due to patient preference for varifocals rather than single vision reading spectacles and not due to a need for full time correction. Difficulty scores were low for everday tasks such as driving and watching TV (Figure 9).

Overall satisfaction was high (> 90% of subjects) in both groups for distance tasks. Satisfaction was greater for the MIOL group at both intermediate and near (Figure 9a~~, 9b~~). Significant differences were found between groups for all near tasks (Figure 9b~~c, 9d~~) and at both visits the monofocal group reported significantly more difficulty using a VDU screen (Figure 9c~~e, 9f~~). However, satisfaction scores were similar for distance tasks such as driving and watching TV.

Subjects were asked to rate the difficulty invoked in general night vision, and with glare, halos, starburst and ghost images (Figure 9dg, 9h). Significant difference between groups were only evident for halos at both visits; MIOL scores were higher but still categorised as low difficulty (between 1 and 3 for all subjects).

The Zeiss (Carl Meditec Ltd) Glare simulator was used and subjects asked to adjust the settings in order to pictorially display halos/glare akin to those they observe at night. 77% of the MIOL group reported halos, compared to just 6% of the IOL group. Halo size and intensity was quantified using the simulator on a scale of 0 (no halo) to 100 (maximum). Results showed a significant difference in halo size reported in the MIOL group (Figure 10)(Supplementary Figure 9).

The MIOL group had a significantly better NAVQ score, consistent with the greater spectacle independence achieved amongst participants in that group (Figure 11)(Supplementary Figure 10).

DISCUSSION

The 2016 Cochrane review[6] highlighted the need for the evaluation of MIOLs using a core set of standardised outcome measures and graded the current certainty of evidence for efficacy as very low to moderate. This RCT aimed to build on the evidence base by evaluating MIOLs using a comprehensive set of standard outcome measures. Participants were recruited from patients

referred for cataract surgery under the UK NHS. As such the subjects did not attend expecting MIOL implantation and were not motivated for achieving spectacle independence which may in fact have biased the results towards spectacle dependence. Conversely, most existing studies of this nature are non-randomised and hence prone to bias towards spectacle independence in addition to influencing IOL selection.[25] In addition the mean age of the subjects in this study represent the oldest population of all of the IOL/MIOL RCTs and is the first where the subjects have a mean age greater than 75. As such, the results provide a generalizable dataset for an older patient base.

Near vision

Good uncorrected near vision is the primary motivation for MIOL implantation but assessing it requires a multifaceted approach. Previous studies have shown good near vision with bifocal IOLs, and improved satisfaction with near tasks and spectacle independence[25-27] When compared with a monofocal IOL the present study demonstrated improved unaided and best distance corrected near vision with a MIOL. These results are further supported by the defocus curve analysis, via both the traditional direct comparison method and through the area and range of focus metrics.[20] Additionally the Radner reading charts showed significantly smaller critical print size was achieved whilst maintaining maximum reading speed in the MIOL group. The subjective perception of near vision was also enhanced in the MIOL group as evident via the observations of the two questionnaires used in this study, (QoV questionnaire[17] and the previously validated NAVQ[18]); no differences in satisfaction scores were identified for the distance and intermediate vision.

It must be noted, in most studies, including this study, an arbitrary reading distance of 40cm was used, this is likely to show optimum reading performance for an IOL that has an addition of +2.50D in the spectacle plane, however higher adds will have optimum acuity at a shorter focal length. Therefore, it is possible that maximum UNVA and DCNVA has not been recorded due to this imposed working distance.

Distance Vision

UDVA, CDVA and the direct comparison method of defocus curve analysis demonstrated no difference in vision at distance between the two lens types. Whilst the distance area-of-focus metric was greater at V1, by V2 both distance areas were similar. However, contrast sensitivity measurements were lower in the MIOL group at visit 1. This is consistent with the findings of other studies [26, 28-33] and is an expected finding with any RCT comparing MIOLs with IOLs. All MIOLS have a near focal point, which creates a myopic blur circle around the distance focal point; it is this blur that affects CS. The MIOL examined in the present study is designed to be distant dominant when viewing a distance object (provided a large pupil is present), this will reduce the intensity of the blur circle minimizing its impact on CS and preserving distance vision quality. By months 12-18 there was no significant difference in CS as measured on the Peli-Robson and at all but the low spatial frequencies on the CSV-1000. Given that there was no significant difference in distance visual acuity, and that the subjective satisfaction of distance vision was comparable, it is probable that the lens design has minimized the impact of the blur circle to the point whereby it is no longer of clinical significance.

Subjects implanted with MIOLs reported halos at both visits according to both the questionnaire data and glare simulator. This is to be expected as these halos are created by the defocus of the second focal point and are present with all MIOLs. The intensity of the halo is an important consideration with MIOL design. Theoretically distance dominant MIOL demonstrate lower halo intensities. The study MIOL incorporates a partially diffractive surface which is distance dominant with large pupil sizes and given that the perception of halos occurs mainly at night it is likely that the impact of halos on vision has been minimized: This may explain how, despite the presence of halos, overall satisfaction with distance vision was high (97%).

Intermediate Vision

Intermediate vision is relatively difficult to define and hence this study has used a variety of methods to assess visual function in this region. The intermediate area-of-focus metric defined by Buckhurst and colleagues[20] and used in this study evaluates vision quality between a defocus of -0.50 to -2.00D (corresponding to a working distance of approximately 0.50 to 2.00m). The intermediate area-of-focus results showed no significant difference between the MIOL and IOL; affirmed by the non-significant finding for intermediate vision using the ETDRS chart at 70cm. The Direct comparison method of defocus curve analysis demonstrated an improved visual acuity with a -2.00D of optical defocus corresponding with a distance of 50cm. This is similar to the findings of Hayashi[34] who found that an MIOL of +3.00D addition vision provided similar acuities to a monofocal IOL at distances of 1.0 and 0.7m whilst better acuities at 0.5 and 0.3m. Hitherto, the only study to have examined the Bi-Flex 677MY MIOL was a non-control cohort study on 25 subjects[27]. Analogous to the present observations the investigators noted similar defocus curves

with a peak in visual acuity at approximately -2.50D of defocus with a similar profile across the intermediate range. Comparability between the present study and this cohort study is limited as only mean defocus curve acuity values were reported and mean age of the cohort was over 10 years younger than that of the present study. Subsequent to the results of this study a revised version of this optic has been designed (the Liberty MIOL), that distributes light to the intermediate zone.

Interestingly, in the present study the perception of quality of vision for computer use was superior amongst the MIOL group; suggesting that improved acuity at 0.5m is sufficient to notice an improvement in in vision for VDU use.

Spectacle independence

67% of the MIOL group were found to be entirely spectacle independent, whilst the remaining 33% of patients only wore glasses occasionally. This is a lower level of spectacle independence than has been recorded in previous studies.[25,28,35,36] Motivation for spectacle independence is likely to be an important factor in these disparate observations; given that in the present study, participants attended for cataract removal rather than for a specific refractive outcome. Individuals with a prior motivation to be spectacle independent are more likely to tolerate near and intermediate blur and hence comparability between studies can be limited.

Only 5% of the monofocal group were found to be spectacle independent with 30% requiring constant correction and the remaining 65% occasionally wearing spectacles. A disparity between the type of spectacles worn was evident between groups, with 35% of subjects implanted with monofocal IOLs wearing either bifocals or varifocals post-operatively when compared to just 3%

of the MIOL group. It is important to note that overall satisfaction of distance vision was similar in both groups whilst satisfaction of near and intermediate vision was considerably greater in the MIOL group with 95% of subjects satisfied.

Unaided near visual acuity is demonstrably improved with the Bi-Flex MY IOL with greater spectacle independence. With regard to visual acuity measures, it must be noted that this study aimed to compare the MIOL and monofocal IOL using a standardised method, with specific lighting levels and working distances for near and intermediate. Limitations in visual performance due to halos, glare and reduction in contrast were evident amongst the MIOL group, and although statistically significant, they do not appear to limit the subject's visual function nor their perception of vision and overall satisfaction. Thus, the study concludes that the Bi-Flex MY multifocal IOL demonstrates efficacy for the correction of near and distance vision and is indicated when improved near vision/spectacle independence is required.

WHAT WAS KNOWN

Multifocal IOLs provide both distance and near vision whereas monofocal IOLs provide image quality at a single distance

Multifocal IOLs cause an increased prevalence of dysphotopsia and result in reduced retinal image contrast

A new Biconvex, aspheric, apodized, diffractive MIOL with a +3.50D add has been designed with a relatively low number of diffractive echelons aimed to improving the optical image quality of the resultant image.

WHAT THIS PAPER ADDS

Distance visual acuity was comparable between the MIOL and IOL. Contrast sensitivity was reduced 3-6 months post-operatively whereas by months 12-18 were similar at all but low spatial frequencies.

Near vision was superior in the MIOL group and subjects in the MIOL group were more satisfied with the quality of vision at near and intermediate.

There was a statistically significant increase in the presence of dysphotopisa in the MIOL group, however, satisfaction with distance vision was high in both groups

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Supplementary Table 1: Inclusion/Exclusion Criteria

Supplementary Table 2: Characteristics of the Intraocular lenses

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Visual Function and Subjective Perception of Vision following bilateral implantation of monofocal and multifocal intraocular lenses: A Randomised Controlled Trial.

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Running Head: Visual Function with MIOLs

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ABSTRACT

PURPOSE:

Following implantation with Multifocal intraocular lenses (MIOLs) or monofocal intraocular lenses (IOLs), the study examines monocular and binocular visual function and patient reporting outcomes using a rigorous series of clinical assessments.

Setting: BMI Southend Hospital, UK

DESIGN: Prospective, randomised, double-masked clinical trial.

METHODS: 100 subjects were randomised for bilateral implantation of either Bi-Flex 677MY MIOL or Bi-Flex 677AB IOL and were assessed at 3-6 months (V1) and 12-18 months (V2). Primary outcomes included distance, intermediate and near LogMAR visual acuities (VA) and defocus curve profile assessment. Secondary outcomes included reading speed, contrast sensitivity (CS) and the subjective perception of quality-of-vision.

RESULTS: Uncorrected (MIOL 0.10±0.09LogMAR; IOL 0.09±0.11LogMAR) and best distance-corrected VA (MIOL 0.04±0.06LogMAR; IOL 0.01±0.07LogMAR) were comparable (p>0.05). Unaided near VA (UNVA p<0.001: MIOL 0.23±0.13LogMAR; IOL 0.55±0.20LogMAR) and distance-corrected near VA (DCNVA p<0.001: MIOL 0.24±0.13LogMAR; IOL 0.54±0.17LogMAR) were significantly improved with MIOLs. There was no significant difference in distance-corrected intermediate VA (DCIVA p=0.431: MIOL 0.38±0.13; IOL 0.39±0.13).

Defocus curves demonstrated an increased range-of-focus amongst MIOLs (MIOL 4.14±1.10D; IOL 2.57±0.77D). Pelli-Robson CS was different at V1 (p<0.001) but similar by V2 (p=0.059).

Overall satisfaction was high (>90%) in both groups for distance tasks whereas significantly different for near (MIOL 18.45±16.53LogUnits; MIOL 55.59±22.52LogUnits).

CONCLUSIONS: Unaided near visual acuity is demonstrably better with MIOLs and there was greater subjective satisfaction with their quality-of-near-vision. Halos reported by the MIOL group was significant compared to the IOL group, but did not show an adverse effect on overall satisfaction.

Multifocal intraocular lenses (MIOLs) are widely considered the most reliable method of achieving spectacle independence following cataract surgery.[1-3] MIOLs distribute the light between distant and near focal points whereby the vergence of the incident light dictates which focal point is conjugate to the retinal plane.

The separation of these multiple focal points is determined by the addition power of the MIOL and to a lesser extent the biometry of the eye. High addition MIOLs (+4.00D or higher) are the zeitgeist of the designs used in the late 90s-early 2000s. Disadvantages of these early lenses included a close working distance and reduced intermediate vision. Moreover, the size of the dysphotopic phenomenon (commonly described as halo), associated with MIOLs, increases according to the addition power; these higher addition lenses generate larger haloes.[4,5]

The light energy distribution between the retinal focal points created by a MIOL influences the overall quality of vision at different viewing distances. MIOLs that split light equally, create two focal points of comparative image quality. In contrast, distance dominant MIOLs allocate a higher

percentage of light towards the distance retinal focal point and consequently near vision is relatively compromised. Conversely, the intensity of the halo is influenced by the light distribution relationship: the more distance dominant the lower the dysphotopic intensity.

In 2016, a Cochrane Review[6] highlighted the need for robust randomised control trials examining the efficacy of MIOLs over monofocal intraocular lens (IOL) implantation and called for standardization of outcome measures in MIOL studies. The review concluded that it was unclear whether the achieved benefits of MIOL implantation i.e. greater near vision and increased spectacle independence, outweighed disadvantages such as reduced contrast sensitivity and increased dysphotopsia. Subsequently others have also highlighted the importance of patient reported outcomes in MIOLs.[7] Despite these conclusions, in the subsequent three years there has only been a single RCT published comparing MIOLs with IOLs.[8]

The present study compared the efficacy of the Bi-Flex 677MY MIOL over its parent monofocal IOL using standardized methods for assessing both visual function and the subjective perception of the quality of vision.

METHODS

This study was a prospective, parallel double masked randomised clinical trial. The study protocol adheres to the Declaration of Helsinki and ethical approval was obtained prior to commencement of the trial. The study was registered with clinicaltrails.gov (NCT02338882) and written consent was obtained from all subjects. No modifications to the protocol or outcome measures were

made during the study. The aim was to assess the IOLs using recognised methods that would provide rigour and establish a comprehensive method which could be utilised with all IOLs and allow easy comparison of results.

Patient Selection

Between September 2015 and May 2017, one hundred subjects were recruited from routine cataract clinics at the BMI Southend Hospital on a consecutive – if – eligible basis according to the inclusion/exclusion criteria (Supplementary Table 1). All subjects underwent initial examination by a consultant ophthalmic surgeon including dilated fundus examination; in the event of suspected macular pathology an OCT was carried out and if pathology was detected, the patient was excluded as per the study criterion. The anterior segments and ocular surface were also evaluated to confirm lack of pathology and minor ocular surface dryness was treated by commencement of ocular lubricants. Any ocular surface disease deemed moderate or marked resulted in exclusion. The allocation of IOLs was randomly designated and was masked to both the participant and the investigator conducting the post-operative study assessments. On enrolment, a study number was assigned to each subject. Using this study number, the allocation of lenses for all subjects was randomized in Microsoft Excel using blocked randomization with a 1:1 allocation ratio. Following allocation of the subject number, the unmasked surgeons and theatre staff accessed the randomization log and a series of sealed opaque envelopes that described which lenses were to be implanted (MIOL or IOL).

Surgical Technique

All surgeries were performed by one of two experienced consultant ophthalmic surgeons (RA and HK) using small incision phacoemulsification. The same surgeon implanted both lenses for an individual subject. In each case, a 2.2mm clear corneal incision was located according to the steepest corneal meridian. The pre- and post-operative medication regime was the same regardless of surgeon. Second eye surgery occurred within 4 weeks of first eye surgery.

Masking

All post-operative study outcome measures were collected by a study investigator, who was masked to the allocation of study group. The subjects were also masked to their grouping allocation and were only informed of the type of lens implanted once they had completed the study. Post-operative slit lamp examination was performed by the unmasked consultant surgeon in order to maintain masking of the study investigator.

Intraocular Lenses

Each group had fifty subjects assigned. The Bi-Flex 677 AB is a single piece, aspheric aberration neutral IOL. The Bi-Flex MY MIOL has the same platform as the monofocal but the anterior surface has a 3mm apodized, diffractive central region with a near addition of 3.50D at the IOL plane (Supplementary Table 2). The Bi-Flex MY MIOL design is intended to provide distance dominance with greater mydriasis, thus maximizing contrast and minimizing halos when driving at night. Pupil miosis changes the light distribution relationship and results in a relatively equal split of light, hence, the Bi-Flex MY MIOL exploits the near miosis that occurs with reading. This type of MIOL was chosen for the study given that the unique aspect of the Bi-Flex MY is its low number of diffractive echelons (seven) which is theorized to improve the optical image quality of

the resultant image. The identical platform and material of the two IOLs allowed unhindered assessment of the multifocality.

Primary Outcomes Measures

A masked investigator assessed the subjects at two study visits, 3-6 months (V1) and 12-18 months (V2) post-operatively. At each visit, monocular and binocular LogMAR acuities for unaided distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) were measured using computerised test charts (Thomson Software Solutions Ltd) at 6m following the Bailey-Lovie principles and employing Sloan letters consistent with testing methods established by the Early Treatment Diabetic Retinopathy Study (ETDRS).[9-13] Subjective refraction was conducted at 6m with a distance fixation target. The assessment of unaided near visual acuity (UNVA), distance corrected near visual acuity (DCNVA) and distance corrected intermediate visual acuity (DCIVA) utilised ETDRS charts for near (40cm) and intermediate (70cm) (Precision Vision) working distances respectively. To further assess intermediate and near vision at a range of distances, defocus profiles were plotted from -5.00D to 1.50D in 0.50D steps.[14] The letters and defocus lenses were randomised between measures and subjects were prompted once using the phrase “can you read any more letters on the line below?”.[15] All measures of visual acuity were performed with illuminance 120 cd/m2 and luminance of 95 lux.

Secondary Outcome Measures

Contrast Sensitivity was assessed binocularly with the CSV-1000 (Precision Vision) calibrated to 2.4m and both monocularly and binocularly using Pelli-Robson charts at 6m (Thomson Software). Radner reading charts were used to assess reading speed at 40cm following the method outlined by Radner using a digital stopwatch.[16] The subjective perception of vision was assessed using a quality of vision questionnaire[17] and NAVQ.[18] The Carl Zeiss Meditec Glare simulator was used to quantify the appearance of halos and glare. All secondary measures were assessed at V1 and V2. The same assessment room was used throughout the study and all secondary tests were carried out by the same masked investigator in photopic light conditions of illuminance 120cd/m^2 and luminance of 95 lux.

Statistical Analysis

The sample size for the study was calculated using G*power3 (University of Dusseldorf). Power calculations were based on a medium effect size (f = 0.30) based on *a-priori* matched paired *t test* design and a desired statistical power of 90% with an error probability of 0.05. Statistical analysis was performed using SPSS software, version 24 (IBM). All data were tested for normality using the Shapiro-Wilks test and visual examination of histogram plots. In all instances $p<0.05$ was considered statistically significant. It order to evaluate effect size, Cohen's d was calculated, with $d > 0.2$, 0.5 and 0.8 corresponding to small, medium and large effect sizes, respectively.

A repeated measures ANOVA was used to establish similarity between right and left eye data for both monofocal and multifocal IOL data. No significant differences were found and as such only right eye data is presented.[19] Where differences were found after repeated measures ANOVA, further pairwise tests were used to compare the monofocal and multifocal groups for all visual

acuity and contrast sensitivity measurements. Conversion of the NAVQ results to a Rasch score allowed significance to be determined with a Wilcoxon rank-sum test.

The Radner reading speed data was fitted with a non-linear regression (exponential rise to a maximum). Maximum reading speed (MRS) was defined as the asymptote of this curve and Critical print size (CPS) was calculated as the value for x (print size) when the reading speed was 95% of the MRS.

$$x = \frac{\text{Log}(1 - (y-c/a)}{b} \qquad \text{equation 1}$$

Three methods were used to describe the defocus curves using the metrics published by Buckhurst et al.[20] After accounting for magnification of the defocus lenses, the direct comparison method determined significance at each level of acuity; a two way repeated measures ANOVA and pairwise comparison was used to determine if there was a significant difference between groups. Subsequently, fitting spline curves to the dataset allowed the calculation of the range-of-focus, determined using 0.3LogMAR as the threshold. Finally, the near, intermediate and distance areas of the curve were calculated using 0.3LogMAR as the upper limit.[20]

RESULTS

Patient Demographics

Ninety subjects completed the study, one subject had a surgical complication (posterior capsular rupture) prior to IOL insertion and was thus excluded from the study. All subjects attended the

initial post-operative assessment with the consultant surgeon 3-4 weeks post-surgery, however nine subjects were lost to follow up thereafter, seven of these were excluded due to failure to attend one or both of their study visits despite repeated requests, one failed to attend due to ill health and the remaining subject was deceased (Figure 1). There were no adverse or serious adverse events reported in any subjects.

There were no significant differences in pre-operative measures between subjects in the monofocal IOL and MIOL groups, $p > 0.05$ in all instances (Supplementary Table 3).

Post-Operative Refraction

For all participants, manifest spherical equivalent (MSE) was calculated and astigmatism was analysed using the power vector method as described by Thibos.[21] The effect of uncorrected astigmatism[22] is known to be detrimental to outcomes and as such vector analysis was used to ensure that astigmatic effect was similar between groups. No significant differences were found between groups ($p > 0.05$) (Supplementary Table 4).

Visual Acuity

Significant differences were found for UNVA ($p < 0.01$) and DCNVA ($p< 0.01$) both monocularly and binocularly at V1 and V2. With near visual acuity being significantly better in the MIOL group. No significant difference was found for intermediate vision (70cm) (Figure 2)(Supplementary Figure 1)(Supplementary Table 5).

Defocus

A two-way repeated measure ANOVA was performed and a significant difference found ($F_{1,28}$ = 131.889 $p < 0.001$). Pairwise comparisons identified that the differences were significant through the defocus range -2.00 to -5.00 ($p < 0.001$) at both visits, monocularly and binocularly (Figure 3)(Supplementary Figure 2). Cohen's D effect size was calculated and remained > 1 throughout this range, thus categorized as a large effect size.

Defocus curves were also analysed using the area under the curve method as previously described.[20] MATLAB R2017b (The Mathworks Inc) curve fitting software was used to fit a spline curve to each data set. The same software was then used to calculate the area below the curve assuming y = 0.3LogMAR. The ranges were divided into distance (-0.5 to +0.5 defocus), intermediate (-0.5 to -2.0D defocus) and near (-2.0 to -4.0D defocus). A cut-off value of 0.3LogMAR was used as this is the UK, European and American binocular visual acuity driving standards.[23,24]

Distance area was significantly greater in the monofocal group at Visit 1 but not at Visit 2, no difference was found in the intermediate area but the MIOL group showed a larger near area at both visits. In addition to the area metrics, range of focus was calculated as the dioptric range where VA was ≥ 0.3 LogMAR, by finding the roots of the spline curve fitted. The MIOL group had a significantly larger range of focus ($p<0.001$) (Figure 4)(Supplementary Figure 2)(Supplementary Table 6).

Reading Speed

There was significantly better critical print size (CPS) and reading acuity achieved in the MIOL group at V1 (p<0.001) and V2 (p<0.001). No significant difference in MRS was found at either visit (p=0.534 V1 and p =0.555 V2) (Figure 5) (Supplementary Figure 4).

Contrast Sensitivity

Monocular and binocular measures of contrast sensitivity with the Pelli-Robson charts showed a significant difference (p<0.001) at Visit 1 with a large effect size demonstrated (Cohen's d = 0.845 and 1.031 respectively) (Supplementary Figure 5). However, at Visit 2, there was no significant difference between groups when tested binocularly (p = 0.059) (Figure 6).

Binocular contrast sensitivity, measured with the CSV-1000, was greater in the IOL group at visit 1 when measured at 3, 6 and 12cpd spatial frequencies (Supplementary Figure 6); this difference was only present for 12 and 18cpd at Visit 2 (Figure 7)(Supplementary Table 7).

Prior to visit 1 no subject underwent YAG capsulotomy whereas by visit 2; in the monofocal group one subject required YAG capsulotomy unilaterally and one bilaterally, and in the multifocal group one subject required YAG capsulotomy unilaterally and three required it bilaterally. No post-operative procedures were preformed, for the correction of residual ametropia, on any of the subjects.

Questionnaire

75% of the MIOL group were completely spectacle independent compared to 6.7% of the monofocal group at Visit1. At Visit 2, 66.7% and 4.7% respectively remained completely spectacle independent (Supplementary Figure 7).

The type of spectacles worn in both groups was different post-operatively compared to pre-operatively with fewer subjects using bifocals or varifocals. Single vision near spectacles (reading only) were the most common refractive correction in both groups. A small proportion of subjects used spectacles for distance; this finding was consistent with the satisfaction results. In addition 2.5% of the MIOL group used varifocal spectacles post-operatively due to patient preference for varifocals rather than single vision reading spectacles and not due to a need for full time correction. Difficulty scores were low for everday tasks such as driving and watching TV (Figure 9).

Overall satisfaction was high (> 90% of subjects) in both groups for distance tasks. Satisfaction was greater for the MIOL group at both intermediate and near (Figure 9a). Significant differences were found between groups for all near tasks (Figure 9b) and at both visits the monofocal group reported significantly more difficulty using a VDU screen (Figure 9c). However, satisfaction scores were similar for distance tasks such as driving and watching TV.

Subjects were asked to rate the difficulty invoked in general night vision, and with glare, halos, starburst and ghost images (Figure 9d). Significant difference between groups were only evident for halos at both visits; MIOL scores were higher but still categorised as low difficulty (between 1 and 3 for all subjects).

The Zeiss (Carl Meditec Ltd) Glare simulator was used and subjects asked to adjust the settings in order to pictorially display halos/glare akin to those they observe at night. 77% of the MIOL group reported halos, compared to just 6% of the IOL group. Halo size and intensity was quantified using the simulator on a scale of 0 (no halo) to 100 (maximum). Results showed a significant difference in halo size reported in the MIOL group (Figure 10)(Supplementary Figure 9).

The MIOL group had a significantly better NAVQ score, consistent with the greater spectacle independence achieved amongst participants in that group (Figure 11)(Supplementary Figure 10).

DISCUSSION

The 2016 Cochrane review[6] highlighted the need for the evaluation of MIOLs using a core set of standardised outcome measures and graded the current certainty of evidence for efficacy as very low to moderate. This RCT aimed to build on the evidence base by evaluating MIOLs using a comprehensive set of standard outcome measures. Participants were recruited from patients

referred for cataract surgery under the UK NHS. As such the subjects did not attend expecting MIOL implantation and were not motivated for achieving spectacle independence which may in fact have biased the results towards spectacle dependence. Conversely, most existing studies of this nature are non-randomised and hence prone to bias towards spectacle independence in addition to influencing IOL selection.[25] In addition the mean age of the subjects in this study represent the oldest population of all of the IOL/MIOL RCTs and is the first where the subjects have a mean age greater than 75. As such, the results provide a generalizable dataset for an older patient base.

Near vision

Good uncorrected near vision is the primary motivation for MIOL implantation but assessing it requires a multifaceted approach. Previous studies have shown good near vision with bifocal IOLs, and improved satisfaction with near tasks and spectacle independence[25-27] When compared with a monofocal IOL the present study demonstrated improved unaided and best distance corrected near vision with a MIOL. These results are further supported by the defocus curve analysis, via both the traditional direct comparison method and through the area and range of focus metrics.[20] Additionally the Radner reading charts showed significantly smaller critical print size was achieved whilst maintaining maximum reading speed in the MIOL group. The subjective perception of near vision was also enhanced in the MIOL group as evident via the observations of the two questionnaires used in this study, (QoV questionnaire[17] and the previously validated NAVQ[18]); no differences in satisfaction scores were identified for the distance and intermediate vision.

It must be noted, in most studies, including this study, an arbitrary reading distance of 40cm was used, this is likely to show optimum reading performance for an IOL that has an addition of +2.50D in the spectacle plane, however higher adds will have optimum acuity at a shorter focal length. Therefore, it is possible that maximum UNVA and DCNVA has not been recorded due to this imposed working distance.

Distance Vision

UDVA, CDVA and the direct comparison method of defocus curve analysis demonstrated no difference in vision at distance between the two lens types. Whilst the distance area-of-focus metric was greater at V1, by V2 both distance areas were similar. However, contrast sensitivity measurements were lower in the MIOL group at visit 1. This is consistent with the findings of other studies [26, 28-33] and is an expected finding with any RCT comparing MIOLs with IOLs. All MIOLS have a near focal point, which creates a myopic blur circle around the distance focal point; it is this blur that affects CS. The MIOL examined in the present study is designed to be distant dominant when viewing a distance object (provided a large pupil is present), this will reduce the intensity of the blur circle minimizing its impact on CS and preserving distance vision quality. By months 12-18 there was no significant difference in CS as measured on the Peli-Robson and at all but the low spatial frequencies on the CSV-1000. Given that there was no significant difference in distance visual acuity, and that the subjective satisfaction of distance vision was comparable, it is probable that the lens design has minimized the impact of the blur circle to the point whereby it is no longer of clinical significance.

Subjects implanted with MIOLs reported halos at both visits according to both the questionnaire data and glare simulator. This is to be expected as these halos are created by the defocus of the second focal point and are present with all MIOLs. The intensity of the halo is an important consideration with MIOL design. Theoretically distance dominant MIOL demonstrate lower halo intensities. The study MIOL incorporates a partially diffractive surface which is distance dominant with large pupil sizes and given that the perception of halos occurs mainly at night it is likely that the impact of halos on vision has been minimized: This may explain how, despite the presence of halos, overall satisfaction with distance vision was high (97%).

Intermediate Vision

Intermediate vision is relatively difficult to define and hence this study has used a variety of methods to assess visual function in this region. The intermediate area-of-focus metric defined by Buckhurst and colleagues[20] and used in this study evaluates vision quality between a defocus of -0.50 to -2.00D (corresponding to a working distance of approximately 0.50 to 2.00m). The intermediate area-of-focus results showed no significant difference between the MIOL and IOL; affirmed by the non-significant finding for intermediate vision using the ETDRS chart at 70cm. The Direct comparison method of defocus curve analysis demonstrated an improved visual acuity with a -2.00D of optical defocus corresponding with a distance of 50cm. This is similar to the findings of Hayashi[34] who found that an MIOL of +3.00D addition vision provided similar acuities to a monofocal IOL at distances of 1.0 and 0.7m whilst better acuities at 0.5 and 0.3m. Hitherto, the only study to have examined the Bi-Flex 677MY MIOL was a non-control cohort study on 25 subjects[27]. Analogous to the present observations the investigators noted similar defocus curves

with a peak in visual acuity at approximately -2.50D of defocus with a similar profile across the intermediate range. Comparability between the present study and this cohort study is limited as only mean defocus curve acuity values were reported and mean age of the cohort was over 10 years younger than that of the present study. Subsequent to the results of this study a revised version of this optic has been designed (the Liberty MIOL), that distributes light to the intermediate zone.

Interestingly, in the present study the perception of quality of vision for computer use was superior amongst the MIOL group; suggesting that improved acuity at 0.5m is sufficient to notice an improvement in in vision for VDU use.

Spectacle independence

67% of the MIOL group were found to be entirely spectacle independent, whilst the remaining 33% of patients only wore glasses occasionally. This is a lower level of spectacle independence than has been recorded in previous studies.[25,28,35,36] Motivation for spectacle independence is likely to be an important factor in these disparate observations; given that in the present study, participants attended for cataract removal rather than for a specific refractive outcome. Individuals with a prior motivation to be spectacle independent are more likely to tolerate near and intermediate blur and hence comparability between studies can be limited.

Only 5% of the monofocal group were found to be spectacle independent with 30% requiring constant correction and the remaining 65% occasionally wearing spectacles. A disparity between the type of spectacles worn was evident between groups, with 35% of subjects implanted with monofocal IOLs wearing either bifocals or varifocals post-operatively when compared to just 3%

of the MIOL group. It is important to note that overall satisfaction of distance vision was similar in both groups whilst satisfaction of near and intermediate vision was considerably greater in the MIOL group with 95% of subjects satisfied.

Unaided near visual acuity is demonstrably improved with the Bi-Flex MY IOL with greater spectacle independence. With regard to visual acuity measures, it must be noted that this study aimed to compare the MIOL and monofocal IOL using a standardised method, with specific lighting levels and working distances for near and intermediate. Limitations in visual performance due to halos, glare and reduction in contrast were evident amongst the MIOL group, and although statistically significant, they do not appear to limit the subject's visual function nor their perception of vision and overall satisfaction. Thus, the study concludes that the Bi-Flex MY multifocal IOL demonstrates efficacy for the correction of near and distance vision and is indicated when improved near vision/spectacle independence is required.

WHAT WAS KNOWN

Multifocal IOLs provide both distance and near vision whereas monofocal IOLs provide image quality at a single distance

Multifocal IOLs cause an increased prevalence of dysphotopsia and result in reduced retinal image contrast

A new Biconvex, aspheric, apodized, diffractive MIOL with a +3.50D add has been designed with a relatively low number of diffractive echelons aimed to improving the optical image quality of the resultant image.

WHAT THIS PAPER ADDS

Distance visual acuity was comparable between the MIOL and IOL. Contrast sensitivity was reduced 3-6 months post-operatively whereas by months 12-18 were similar at all but low spatial frequencies.

Near vision was superior in the MIOL group and subjects in the MIOL group were more satisfied with the quality of vision at near and intermediate.

There was a statistically significant increase in the presence of dysphotopisa in the MIOL group, however, satisfaction with distance vision was high in both groups

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Supplementary Table 1: Inclusion/Exclusion Criteria

Supplementary Table 2: Characteristics of the Intraocular lenses

Supplementary Table 3: Patient Demographics

Supplementary Table 4: Refraction

Supplementary Table 5: Visual Acuity Results

Supplementary Table 6: Area Under Defocus

Supplementary Table 7: CSV-1000

Figure 1: Trial Profile

Figure 2: a) Visit 2 Monocular Visual Acuity, b) Visit 2 Binocular Visual Acuity

Figure 3: a) Visit 2 Monocular Defocus Curve, b) Visit 2 Binocular Defocus Curve

Figure 4: a) Visit 2 Area under defocus curve, b) Visit 2 Range of focus

Figure 5: a) Visit 2 Maximum Reading Speed, b) Visit 2 Reading Acuity, c) Visit 2 95% Critical Print Size

Figure 6: a) Visit 2 Monocular Contrast Sensitivity, b) Visit 2 Binocular Contrast Sensitivity

Figure 7: Visit 2 CSV-1000 Contrast sensitivity

Figure 8: Spectacle Wear a) Visit 2 Frequency of wear, b) Visit 2 Type of spectacles, c) Pre-Op spectacle wear

Figure 9: Quality of Vision Questionnaire results a) Visit 2 Satisfaction, b) Visit 2 Near Tasks, c) Visit 2 Everyday Tasks, d) Visit 2 Night Vision

Figure 10: Visit 2 Glare Simulator Scores

Figure 11: Visit 2 NAVQ Scores

Supplementary Figure 1: a) Visit 1 Monocular Visual Acuity, b) Visit 1 Binocular Visual Acuity

Supplementary Figure 2: a) Visit 1 Monocular Defocus Curve, b) Visit 1 Binocular Defocus Curve

Supplementary Figure 3: a) Visit 1 Area under defocus curve, b) Visit 1 Range of focus

Supplementary Figure 4: a) Visit 1 Maximum Reading Speed, b) Visit 1 Reading Acuity, c) Visit 1 95% Critical Print Size

Supplementary Figure 5: a) Visit 1 Monocular Contrast Sensitivity, b) Visit 1 Binocular Contrast Sensitivity

Supplementary Figure 6: Visit 1 CSV-1000 Contrast sensitivity

Supplementary Figure 7: Spectacle Wear a) Visit 1 Frequency of wear, b) Visit 1 Type of spectacles

Supplementary Figure 8: Quality of Vision Questionnaire results a) Visit 1 Satisfaction, b) Visit 1 Near Tasks c) Visit 1 Everyday Tasks, d) Visit 1 Night Vision

Supplementary Figure 9: Visit 1 Glare Simulator Scores

Supplementary Figure 10: Visit 1 NAVQ Score

Randomised control trial comparing visual and subjective satisfaction with monofocal and multifocal intraocular lenses (MIOLs). Results demonstrated greater near vision and satisfaction with MIOLs and equivocal distance acuity and satisfaction

Figure 7

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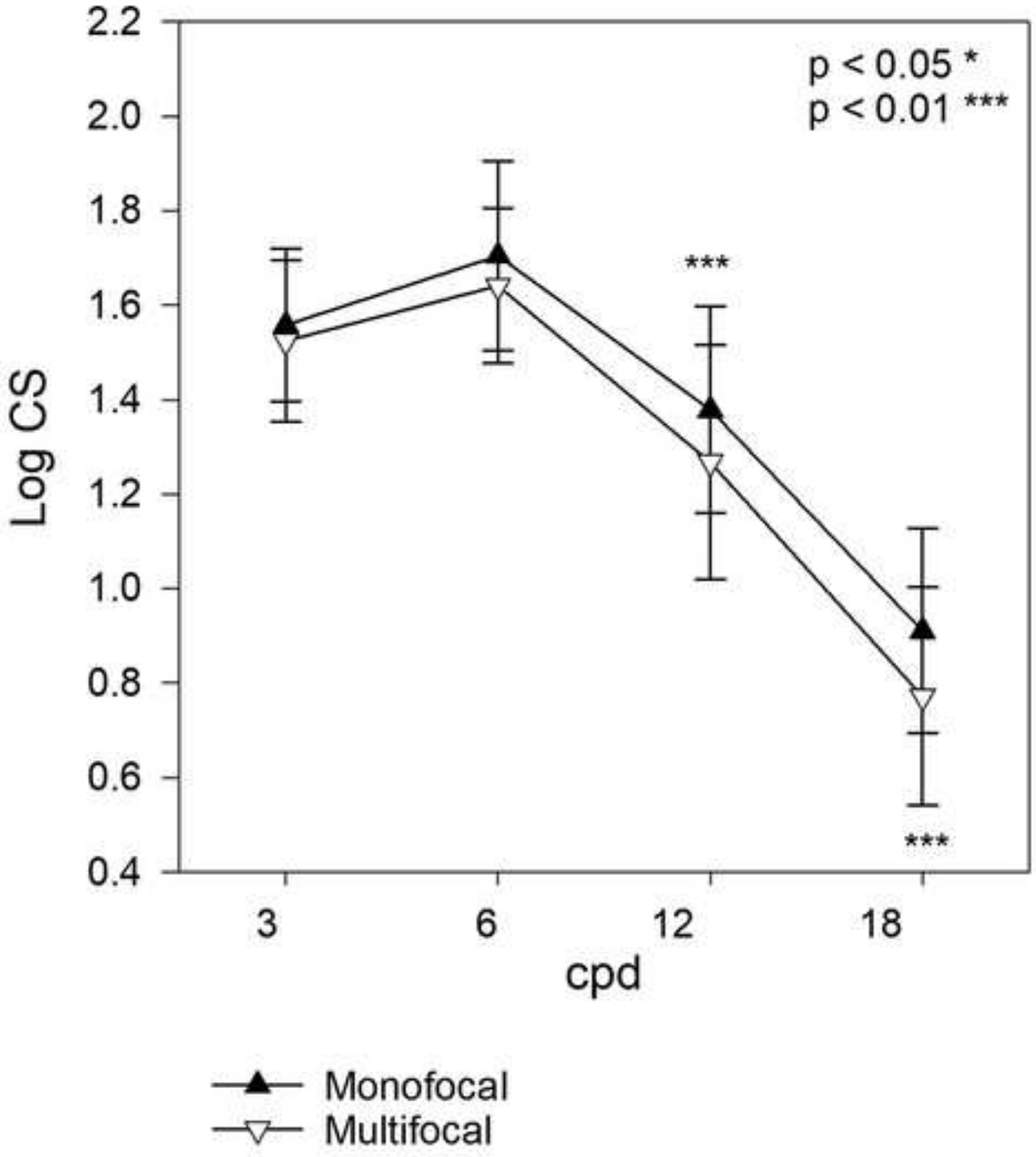

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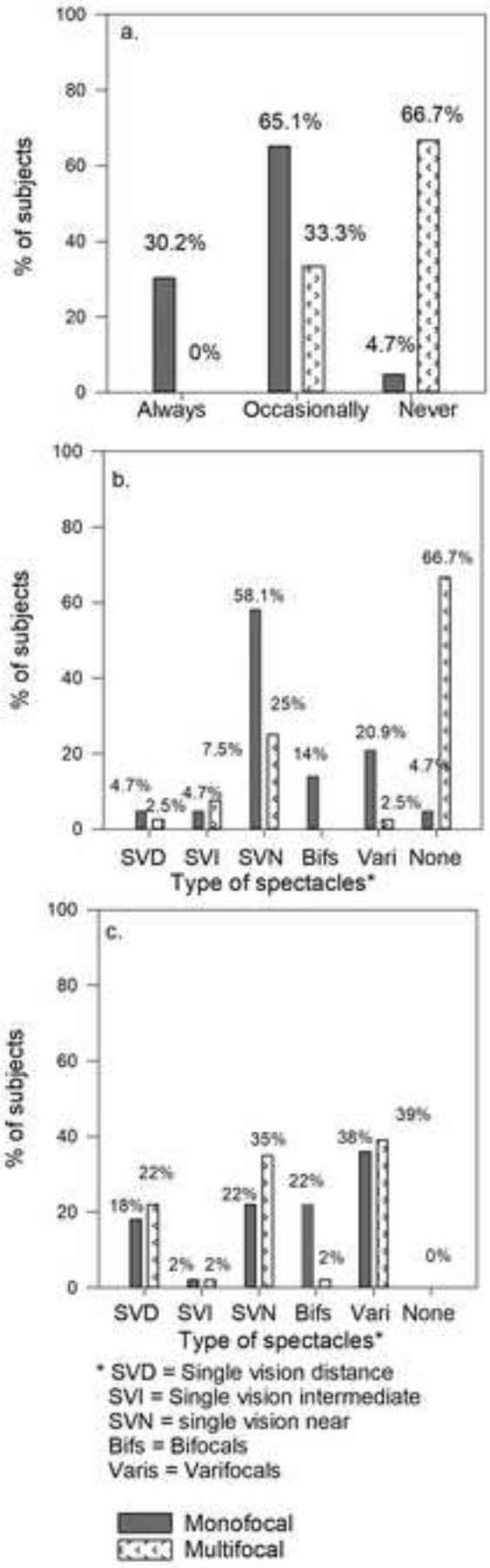

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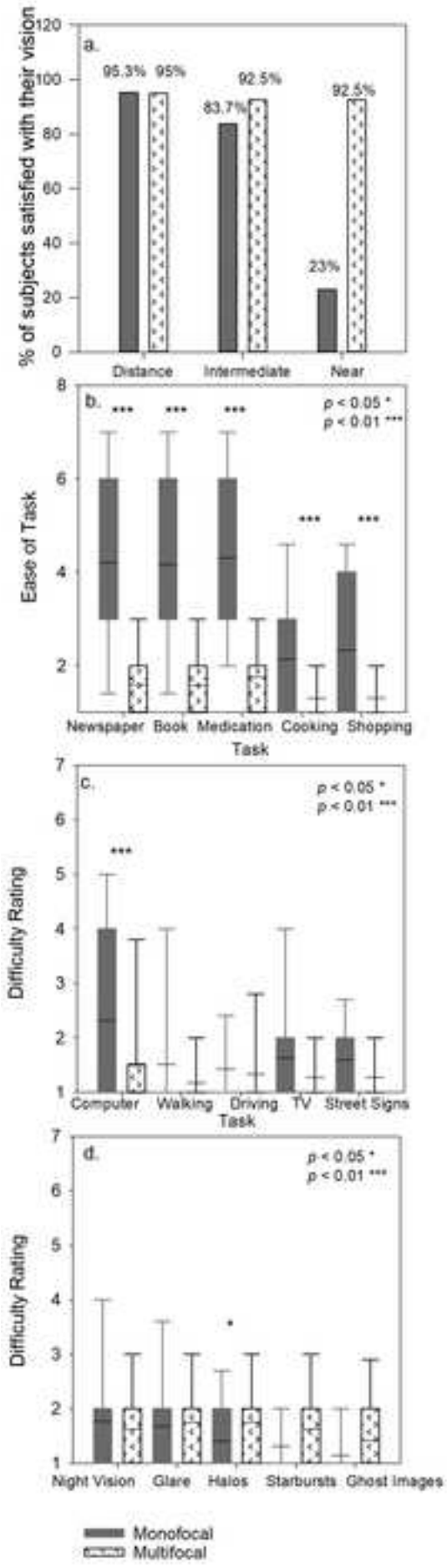

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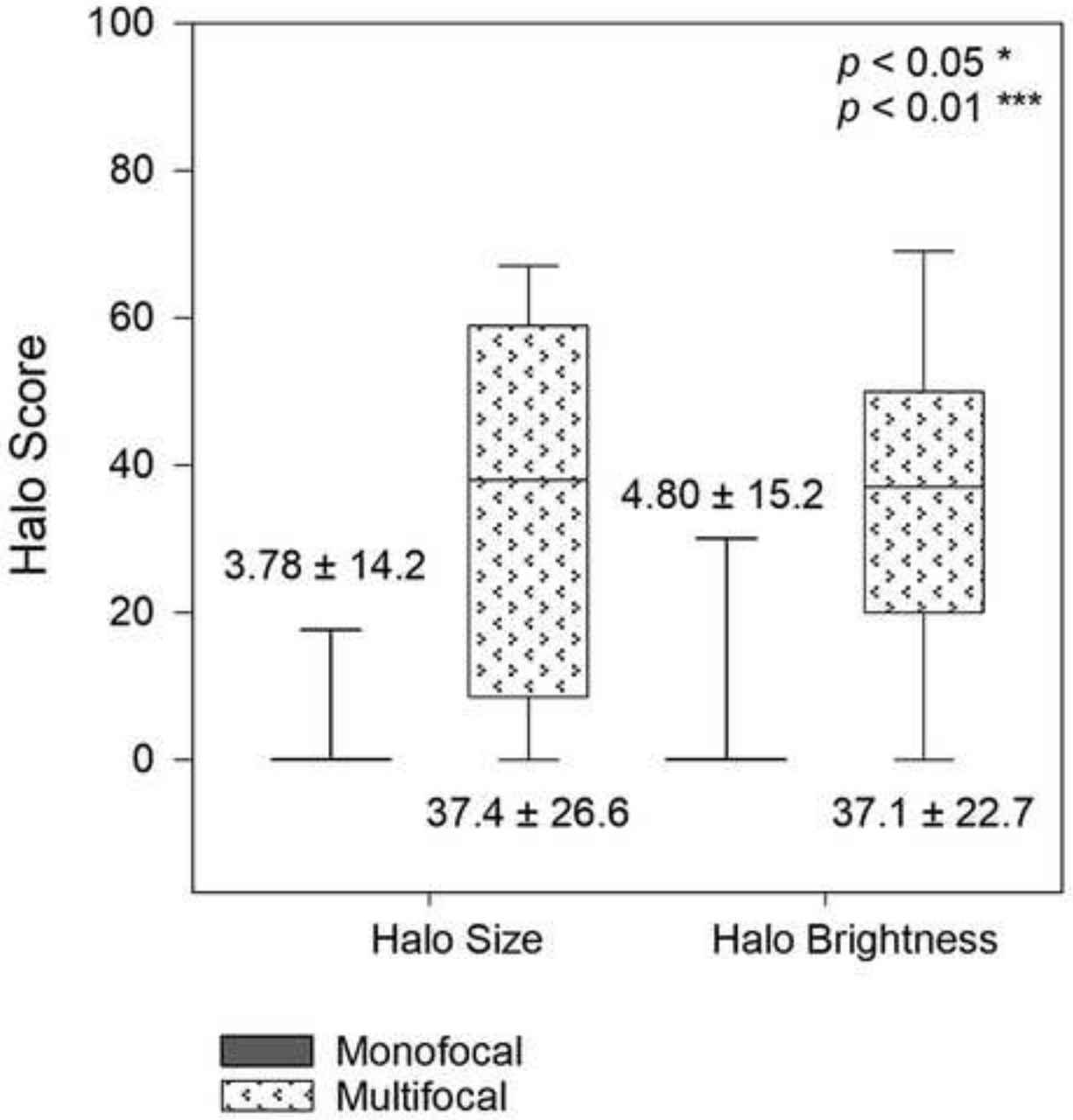

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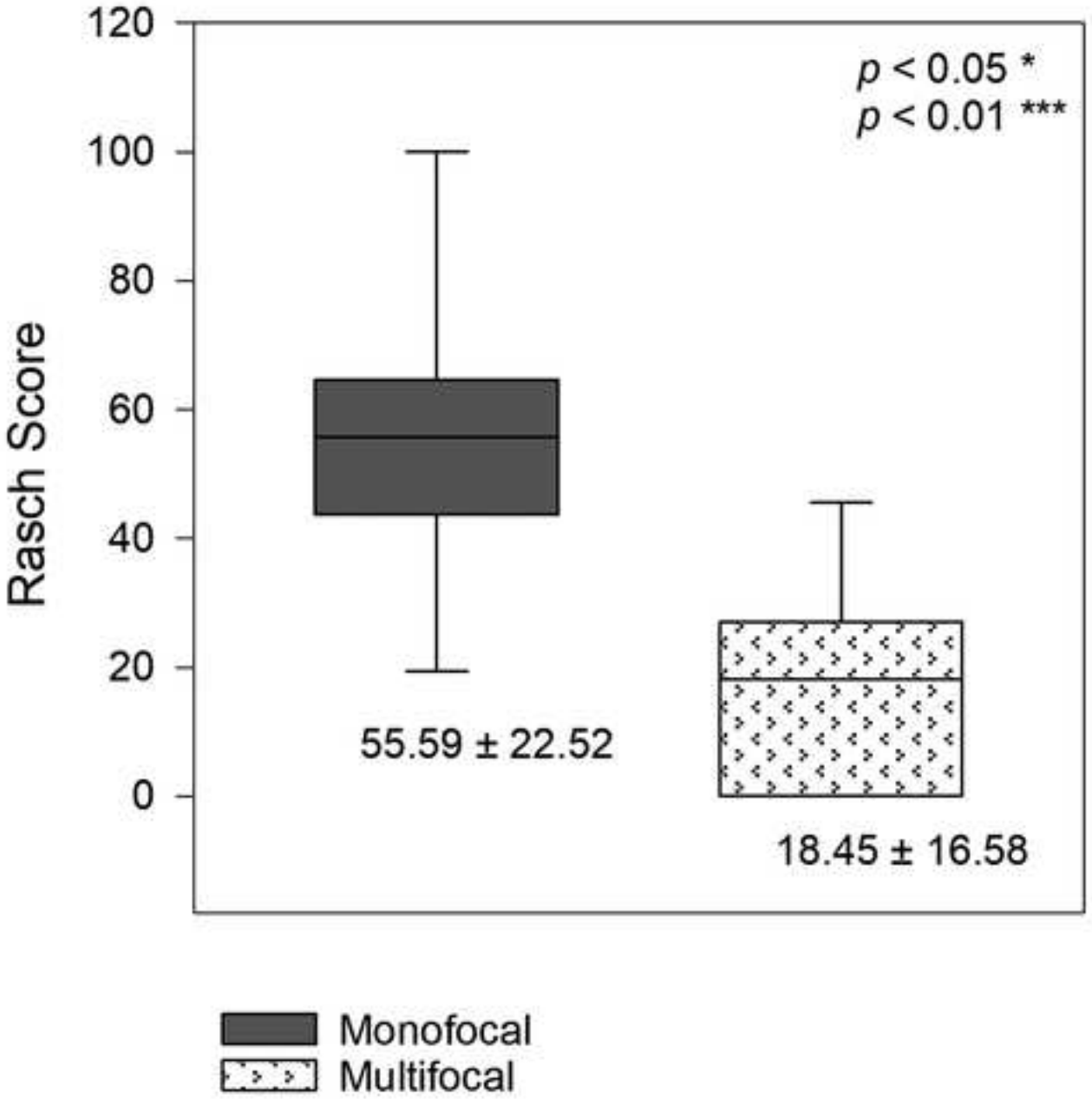

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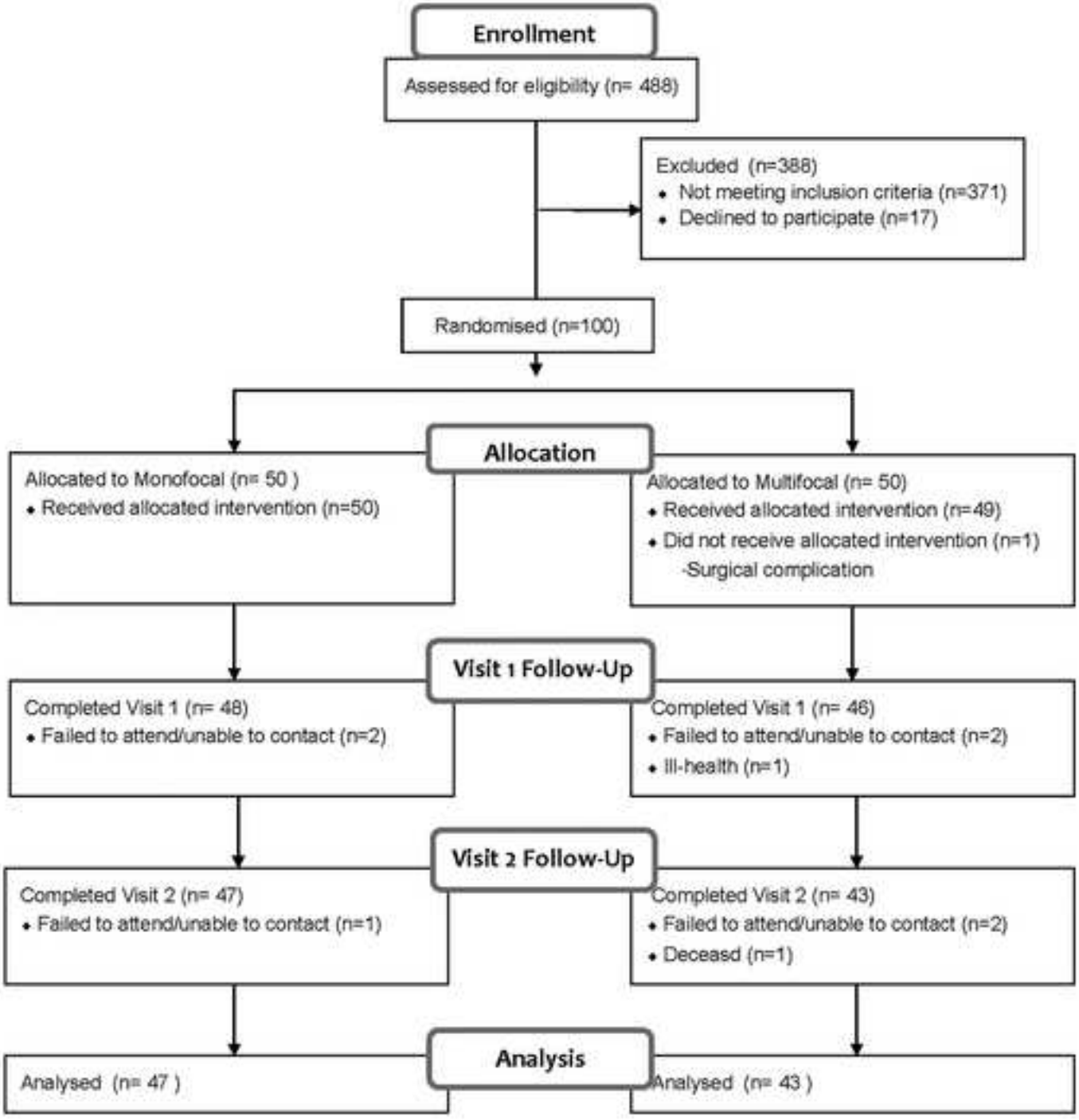

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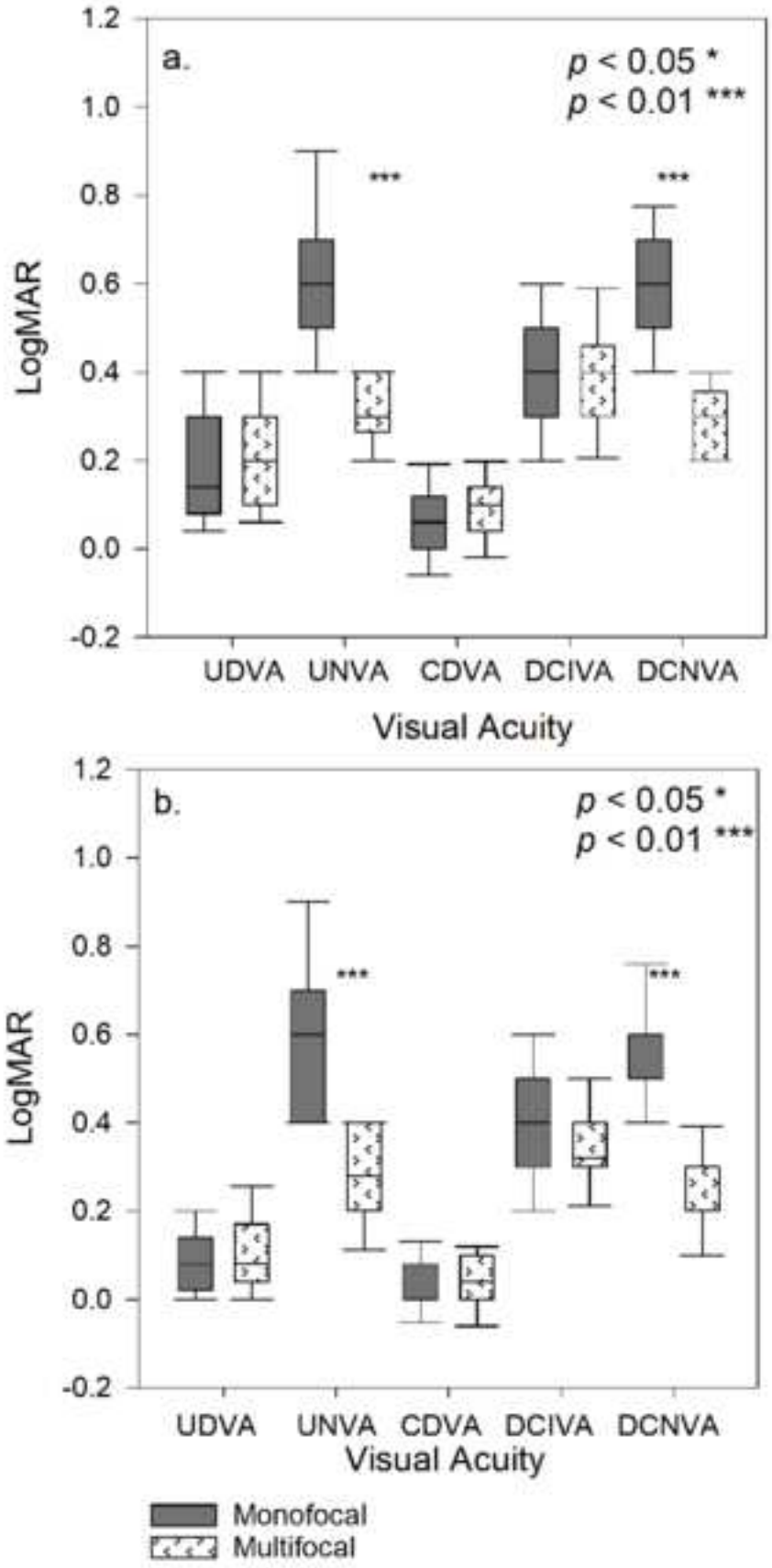

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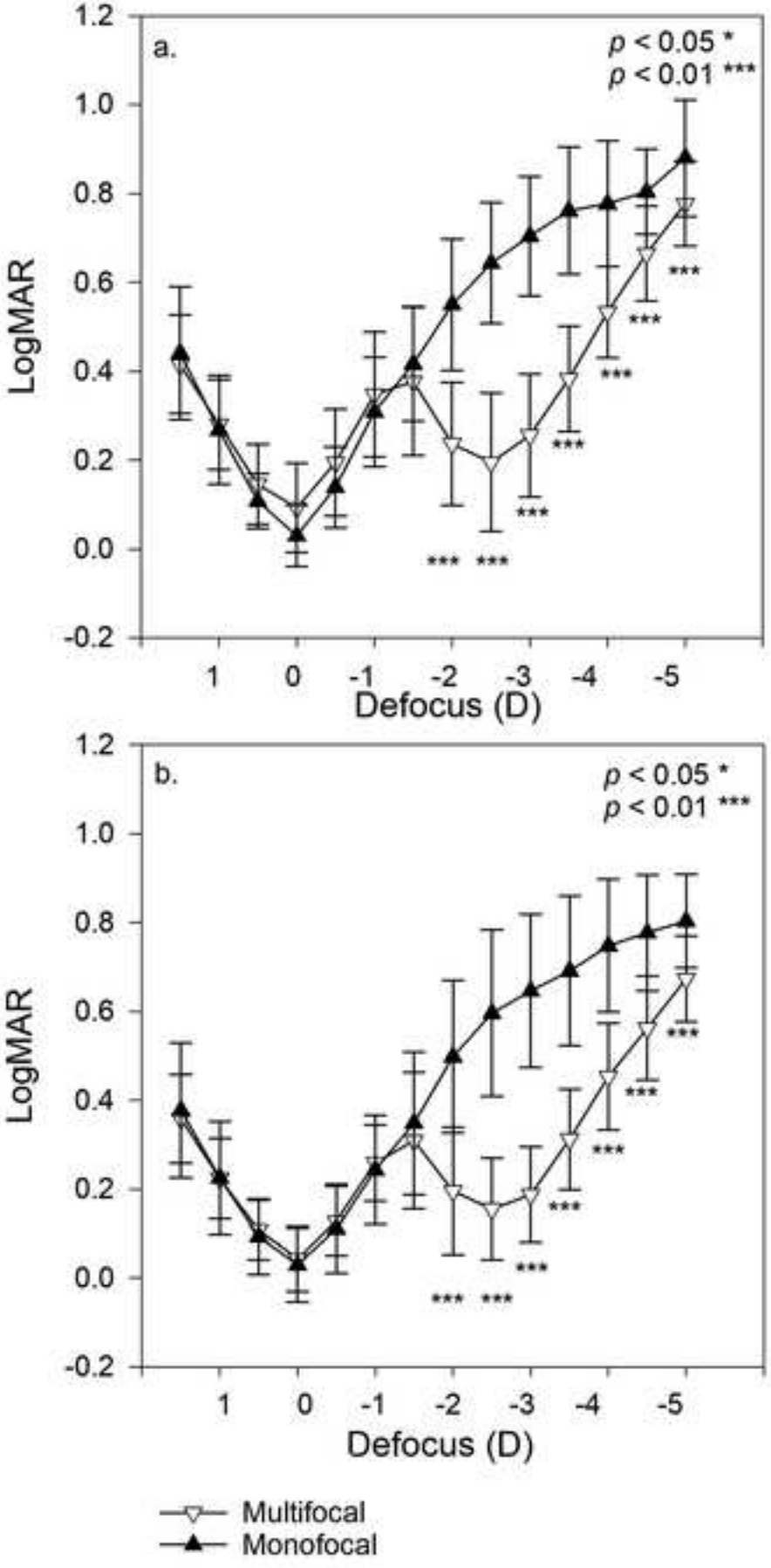

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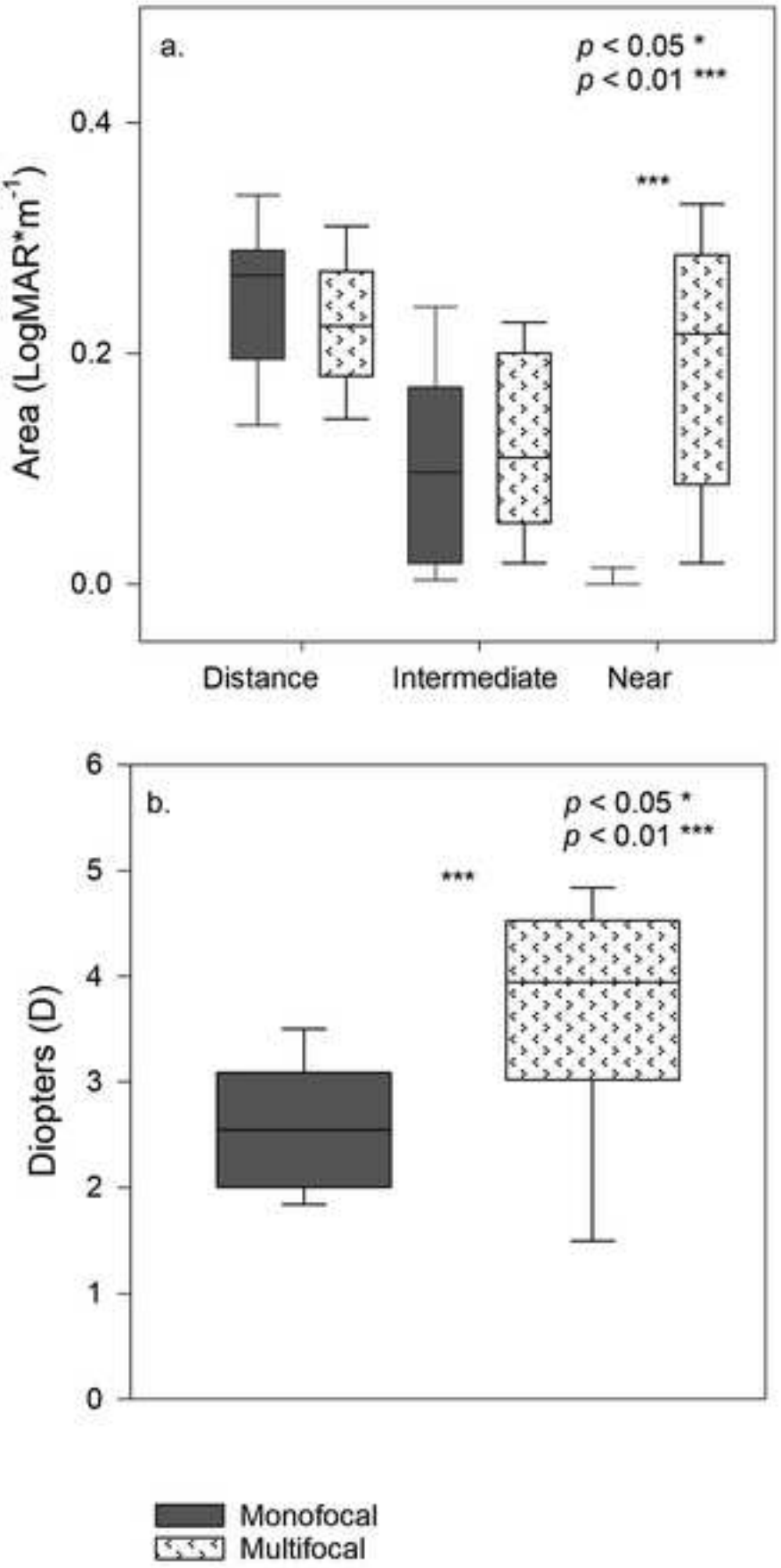

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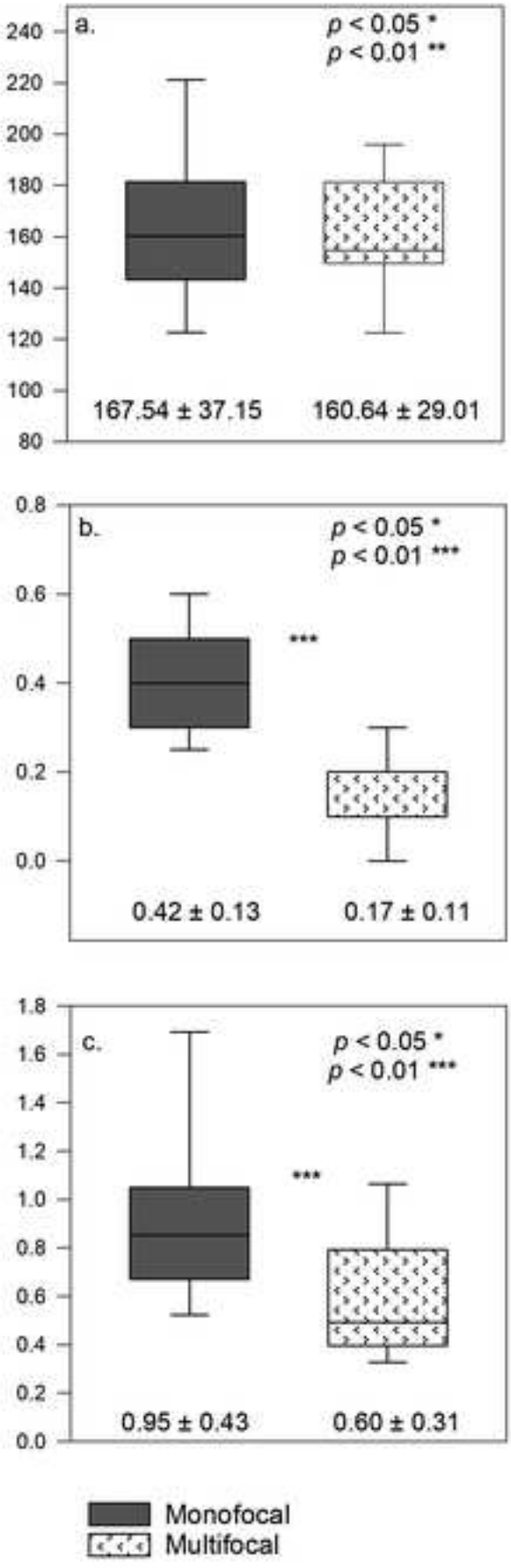

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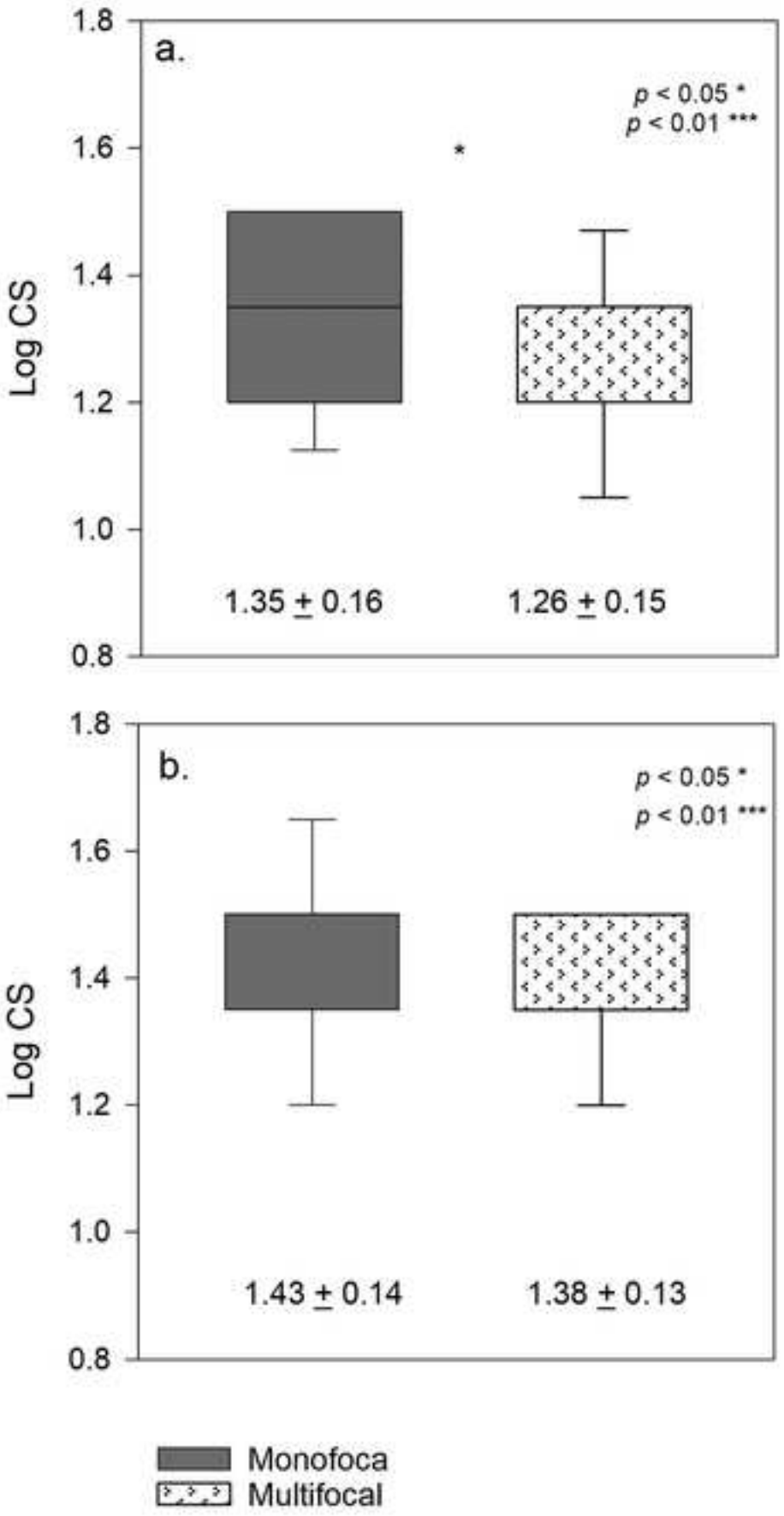

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Supplementary Table 1

Supplementary Table 2

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Supplementary Table 5

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Article Title: Visual Function and Subjective Perception of Vision following bilateral implantation of monofocal and multifocal intraocular lenses: A Randomised Controlled Trial

I have made substantive intellectual contributions to the content of this manuscript in the following areas:

Author Name	Concept and design	Data acquisition	Data analysis / interpretation	Drafting manuscript	Critical revision of manuscript	Statistical analysis	Securing funding	Admin, technical or material support	Supervision	Final approval
Elizabeth M. Law	Y	Y	Y	Y	Y	Y	Y	Y		Y
Rajesh K. Aggarwa	Y	Y	Y		Y		Y	Y		Y
Hetal Buckhurst	Y		Y	Y	Y	Y	Y	Y	Y	Y
Hosam E. Kasaby	Y	Y	Y		Y			Y		Y
Jonathan Marsden	Y				Y	Y			Y	Y
Gary Shum	Y		Y		Y				Y	Y
Phillip J. Buckhust	Y		Y	Y	Y	Y	Y	Y	Y	Y

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